In the Figures:

Please replace Figure 1 as filed with corrected Figures 1A-1C attached hereto as **Exhibit A.**

Please replace Figure 3 as filed with corrected Figures 3A-3C attached hereto as **Exhibit B.**

Remarks

Claims 1-23 are pending in the subject application. Applicants have hereinabove canceled claims 2 and 3 without disclaimer or prejudice, and amended claims 1, 4, 5, 6, 7, 11 and 12. Support for the amendment to claim 1 may be found *inter alia* on page 5, lines 26-30; and page 6, lines 1-18. The amendments to claims 4-7 are made to conform the language of these claims to the scope of claim 1 as amended. Support for the amendments to claims 11 and 12 may be found *inter alia* on page 7, line 2, line 6 and line 12; page 8, line 4, line 10, line 17, line 20 and line 23; page 10, line 27; and page 11, line 7 and lines 13-15. Applicants maintain that none of the amendments to the claims raises an issue of new matter. Therefore, entry of this amendment is respectfully requested. Upon entry of this amendment, claims 1, 4-7, 11 and 12 as amended will be pending and under consideration.

Claim Rejections Under 35 U.S.C. §101

On page 3 of the July 17, 2006 Office Action, the Examiner rejected claims 11 and 12 because the claimed invention is allegedly directed to non-statutory subject matter. The Examiner stated that the claims fail to include any limitations which would distinguish the claimed polynucleotides from those which occur in nature. The Examiner stated that in the absence of the hand of man, the naturally occurring nucleic acid molecules and proteins are considered non-statutory subject matter. The Examiner asserted that filing of evidence of a new utility imparted by the increased purity of the claimed invention and amendment of the claims to recite a purity limitation, if supported by the specification, is suggested to obviate this rejection.

In response, but without conceding the correctness of the

Examiner's ground of rejection, applicants note that, as amended, claims 11 and 12 recite "a purified polynucleotide." In addition, as discussed further below the polynucleotides of claims 11 and 12 as amended here, have utility *inter alia* for diagnosis of stroke. Accordingly, applicants maintain that amended claims 11 and 12 satisfy the requirements of 35 U.S.C. §101, and request that the Examiner reconsider and withdraw this ground of rejection.

On pages 3-4 of the July 17, 2006 Office Action, the Examiner further rejected claims 1-9, 11 and 12 because the claimed invention allegedly is not supported by either a specific and substantial credible asserted utility or a well-established utility. The Examiner further alleged that the instant application has provided a description of an isolated DNA encoding a protein and protein encoded thereby. The Examiner further indicated that the instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect.

The Examiner indicated that, in the instant application, it is clear that the protein described therein is what is termed an "orphan protein" in the art. The DNA of the instant application has been isolated because of its similarity to a known DNA. The Examiner further indicated that there is little doubt that, after complete characterization, this DNA and encoded protein may be found to have a specific and substantial credible utility. The further characterization if part of the act of invention and until it has been undertaken, applicants' claimed invention is incomplete.

Further on pages 4-5 of the July 17, 2006 Office Action, the Examiner alleged that, the instant claims are drawn to an

isolated nucleic acid molecules encoding a polypeptide of as yet undetermined function or biological significance. The Examiner indicated that, in the instant specification, the claimed novel nucleic acid molecules of SEQ ID NO: 1 and SEQ ID NO: 3 encode a polypeptide designated STR50 which, on page 5 of the specification, is asserted to be "modulated as a result of neurotoxic stress". The Examiner noted that on page 8 of the Specification "the inventors suggest that STR50 is involved in the apoptosis of cells which accompanies neurotoxic events; it would therefore be beneficial to inhibit STR50 in diseases where such apoptosis is detrimental, and enhance STR50 in diseases where such apoptosis is beneficial". The Examiner further asserted that, in the instant specification, it is stated that the instant STR50 molecules can be used to treat different pathological conditions which include neurodegenerative diseases, ischemia, cardiac arrest, spinal cord trauma and metastatic or primary tumors. Finally, the Examiner indicated that the working examples present in the instant specification are limited to the disclosure of 1. isolation and purification of STR50; 2. pattern of upregulation of expression of STR50 during experimental shock/ischemic conditions; and 3. prophetic protocols explaining how to use STR50 gene or polypeptide in screening assays and pharmaceutical formations.

The Examiner further indicates on page 5 of the July 17, 2006 Office Action, that in the absence of knowledge of the biological significance of this specific nucleic acid and encoded protein, there is no immediately obvious patentable use for the polynucleotide or the encoded protein. The Examiner alleged that, the instant specification fails to provide any factual evidence or sound scientific reasoning to support a conclusion that the instant nucleic acid or encoded protein is associated with any disease or disorder, including pathological conditions specifically recited on pages 15-17 of the disclosure. The

Examiner further alleged that, the instant application failos to demonstrate use of the claimed STR50 polynucleotides as a marker for any disease or condition. Because the instant specification does not teach a biological activity of the protein, which supports a practical utility, one would not reasonably believe that the administration of the STR50 encoded by the claimed nucleic acid molecules would prevent or treat a condition or disease, like for treating a neurodegenerative disease, stroke or cancer. The Examiner asserted that to employ a nucleic acid of the instant invention in any of the disclosed methods would clearly be using it as the object of further research, which alone does not support patentability. Therefore, since the instant specification does not disclose a credible "real world" use for the encoded protein in their currently available form, the claimed invention is incomplete and does not meet the requirements of 35 U.S.C. §101 as being useful.

In response, applicants respectfully traverse the Examiner's grounds of rejection.

First, applicants point out that at least one specific utility for applicants' polynucleotides as now claimed is for diagnosis. Applicants note that, contrary to the Examiner's assertion, the gene was not isolated based on sequence homology, but was experimentally identified as a gene which has differential expression in stroke, as noted in Example 1 of the specification. Expression of the STR50 gene expression arose after experiments which stimulate stroke, and the diagnostic utility of applicants' claimed polynucleotides for stroke is specific, substantial and credible. Further support for the diagnostic utility of the polynucleotides and polypeptides can be found on pages 19-20 of the specification.

In view of the preceding remarks, applicants maintain that claims 1-9 and amended claims 11-12 satisfy the requirements of 35 U.S.C. §101 and request that this ground of rejection be reconsidered and withdrawn.

Claim Rejections Under 35 U.S.C. §112, First Paragraph

On page 6 of the July 17, 2006 Office Action, the Examiner rejected claims 1-9, 11 and 12 under 35 U.S.C. §112, first paragraph, as allegedly not enabled because the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, and therefore one skilled in the art would not know how to use the claimed invention. The Examiner further rejected claims 2-5, 11 and 12, under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(S) at the time the application was filed had possession of the claimed invention.

On page 7 of the July 17, 2006 Office Action, the Examiner indicated that claims 2-5 are directed to nucleic acids that are homologs of polynucleotides of SEQ ID NO: 1 and 3 or fragments 644 to 3109 of SEQ ID NO: 1 and SEQ ID NO: 3. The Examiner further stated that claims 11 and 12 encompass fragments of 10 to 766 or to 922 consecutive nucleotides within sequence of SEQ ID NO: 1 and SEQ ID NO: 3, respectively. The Examiner alleged that because the claims do not require that the polynucleotides or their fragments possess any particular conserved structure or other disclosed distinguishing feature, the claims are drawn to a genus of polynucleotides that is defined only by structural similarity. Further, the Examiner alleged that the instant application fails to describe the entire genus of nucleic acid molecules encompassed by claims 11 and 12.

The Examiner indicated that from the specification it is clear that the applicants possess nucleic acid molecules which encode proteins which have either SEQ ID NO: 2 or 4 as the amino acid sequence. The nucleic acid molecules have a nucleic acid sequence of either SEQ ID NO: 1 or SEQ ID NO: 3, respectively. The Examiner asserted that the claims are drawn to nucleic acid molecules that are homologs and fragments of these disclosed polynucleotides of SEQ ID NO: 1 and SEQ ID NO: 3 and are therefore not limited to a nucleic acid with a specific sequence. The Examiner further asserted that the instant claims only require the claimed polynucleotides to share some degree of structural similarity to the polynucleotides of SEQ ID NO: 1 and SEQ ID NO: 3. However, the specification only describes a polynucleotide of SEQ ID NO: 1 and a polynucleotide of SEQ ID NO: 3 and therefore failsto teach or describe any other nucleic acid sequence which lacks the sequence of SEQ ID NO: 1 or SEQ ID NO: 3 and has any relevance to STR50 protein.

On pages 8-9 of the July 17, 2006 Office Action, the Examiner alleged that, in the instant case, the only factor present in the claims is a partial structure in the form or a recitation of "homology" or length of fragment and it is therefore unclear what region of the encoded polypeptide has the disclosed activity. The Examiner further alleged that the absent of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Only polynucleotides comprising the nucleic acid sequence set forth in SEQ ID NO: 1 and SEQ ID NO: 3 meets the written description requirement of 35 U.S.C. §112, first paragraph.

In response to the Examiner's rejection, but without conceding the correctness thereof, applicants point out that they have canceled claims 2 and 3 without disclaimer or prejudice, and

amended claims 1, 4, 5, 6, 7, 11, and 12.

In light of the cancellation of claims 2 and 3, and the amendments made, applicants maintain that now pending claims 1, 4-7, 11 and 12 satisfy the requirements of 35 U.S.C. §112, first paragraph, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claim Rejections Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 1, 8 and 9 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the Examiner alleged that claim 1 is indefinite insofar as it employs the term STR50. The Examiner indicated that the term appears to be novel to the instant invention but the Examiner alleged that without reference to a precise amino acid sequence identified by a proper SEQ ID NO: one cannot determine the metes and bounds of STR50. The Examiner further alleged that because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a STR50, an artisan cannot determine if a compound which meets all the limitations of a claim would then be included or excluded from the claimed subject matter by the presence of the limitation. The Examiner further alleged that claims 8 and 9 are indefinite for being dependent from an indefinite claim.

In response to the Examiner's rejection, but without conceding the correctness thereof, applicants have amended claim 1 and have replace "STR50" with "a polypeptide the sequence of which is set forth in SEQ ID NO:2 or SEQ ID NO:4". By this amendment, claim 1 now recites precise amino acid sequences, namely, SEQ ID NO:2 and SEQ ID NO:4. Claims which depend from amended claim 1 also now

recite the precise amino acid sequences recited in claim 1, i.e. SEQ ID NO:2 or SEQ ID NO:4.

In light of the amendments to the claims and the above remarks, applicants maintain that now pending claims 1, 4-9, 11 and 12 satisfy the requirements of 35 U.S.C. §112, second paragraph, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claim Rejection Under 35 U.S.C. §102

The Examiner rejected claims 11 and 12 under 35 U.S.C. §102(e) as allegedly anticipated by Young et al., U.S. Patent No. 6,525,174, 2003 filed December 4, 1998. The Examiner asserted that claims 11 and 12 encompass fragments of polynucleotides of SEQ ID NO: 1 and SEQ ID NO: 3 as short as 10 consecutive nucleotides. The Examiner further indicated that the patent of Young et al. discloses nucleotide sequences that have at least 29.6% sequence similarity, with 98.2% local similarity to the instant SEQ ID NO: 3 and therefore Young et al. anticipate the instant claimed invention of claims 11 and 12.

In response to the Examiner's rejection, applicants respectfully traverse. The reference that the Examiner relies upon is no longer relevant because the sequences of Young et al. are not encompassed by claims 11 and 12 as amended. The sequence in Young et al. referred to by the Examiner commences at nucleotide 1326. The instant claims refer to nucleotides 1-922 (SEQ ID NO: 2) and 1-766 (SEQ ID NO: 3).

In light of the above remarks, applicants maintain that amended claims 11 and 12 are not subject to rejection under 35 U.S.C. §102(e), and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Supplemental Information Disclosure Statement

In order to ensure compliance with applicants' duty of disclosure under 37 C.F.R. §1.56 and §1.97(a)-(d), applicants submit this Information Disclosure Statement as a supplement to the Information Disclosure Statement filed on January 26, 2004. Applicants request that the following document be considered:

1. Letter from Andrew Chin dated April 12, 2004, referring to Andrew Chin's CD-ROM entitled "On the preparation and utilization of isolated and purified oligonucleotides," which Mr. Chin alleges he produced on March 9, 2002 and contributed to a public collection of the Kathrine R. Everett Law Library of the University of North Carolina on March 14, 2002.

A copy of document number 1 is attached hereto as **Exhibit 1**.

According to applicants who have reviewed Mr. Chin's CD-ROM, it contains at least 30,000 pages of printed material which purportedly relate to oligonucleotides between 8 and 12 nucleotides in length, whereas applicants' claimed invention now recites oligonucleotides at least 15 nucleotides in length. Applicants understand that Mr. Chin's CD-ROM cannot be submitted to the Patent Office, but are prepared to submit it if the Examiner so desires.

Summary

For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of rejection set forth in the July 17, 2006 Office Action, and earnestly solicit allowance of the claims as amended herein.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed $450.00 fee for a two-month extension of time is deemed necessary in connection with the filing of this Amendment and Supplemental Information Disclosure Statement. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

12/18/06
John P. White Date
Reg. No. 28,678

Respectfully submitted,

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EXHIBIT A

REPLACEMENT SHEET

Figure 1A – Human STR_50E1 – SEQ ID NO:1

Nucleotide sequence of long splice variant

[initiation ATG and stop codons are underlined]

```
GGGCTCCCTG CACAAATGCG TTGGGTGATG GGGGCTGAAT CCAGCCCACA CTGCACTTGC CAAGCCAGCT   70
GGGGCCCTGG CACAAGACAG TCCCAGCCTG TTTTCACTGA CTTTGCTAAT TCTCACGGAG GCACCATGTG  140
GTGTGGGAAG GCCCGGTCCT CGTAACCTCT CTGCTCCCAG GTCCCTGACC AGTCCTTAAC ACACAGTGGT  210
CTTTGCTCAC CTGCGGCCCA GCTCTGGGCT CTCCCCACAG CATCCTTTGC CTTGCCTCCC TCCCATCTTC  280
CTCTGGGCCT TCTCTCTGCT CCTGCCCAGG AAACTGTGCT CTCAGGAGCG CAGGAGCCAG CTCTCAGCCC  350
CCATCTCCTG GGCACTCACC GTACTCAGGA AATATGTTCT GAATTCAGGA TTATCCTCAT TCTACTGAGA  420
AGACCTGGAG GACAGAAATC AGCAAGACCT AAAGGGGAGA GGAAGGAGGG CCAGGCTGGG GTGGAGGTGC  490
CCCACCCGGG AGCCCGGGCG CAGCCTCACC GCAGGCTGAT TCACAGAAGG CTCAGAGGGT TGCGAGGGCC  560
CAATCGGCAC TGTCATCCTG CCCAGGCTCT GAGTCACCAG CTGGTGAGGG GCAGCTGCAG CCCAGCAGGA  630
AACAAAGTCT AGCATGGAAG AGGTGGGAGG GAGGTGGTGG GGCCTGAAAC CCCGCCTGGC TGGCCTTAGA  700
GGAACTGGGA GTGACTGTCC GGCACTGGCT CAGCAGCAAA CAGCTCTCAA GGACGTGCTA GGAGTCAGGA  770
ACTGGGCCAG CTCCGGTCCC TTCCTTTTGG GGCTCTCACT CTGGAGGATG GGGTGGATGG GAGGTCAGAG  840
GAGCACCAGC CTATGGCCCT GGACACCTGG GGTATTCAGC GAGTTCCTGG AGGACGGTGG GATGGGGCTG  910
TGGTTCCAGC AAGAAAAAAC CGGGAAGATC CTGACGGAGT TCCTCCAGTT CTATGAAGAC CAGTATGGCG  980
TGGCTCTCTT CAACAGCATG CGCCATGAGA TTGAGGGCAC GGGGCTGCCG CAGGCCCAGC TGCTCTGGCG 1050
CAAGGTGCCA CTGGACGAGC GCATCGTCTT CTCGGGGAAC CTCTTCCAGC ACCAGGAGGA CAGCAAGAAG 1120
TGGAGAAACC GCTTCAGCCT CGTGCCCCAC AACTACGGGC TGGTGCTCTA CGAAAACAAA GCGGCCTATG 1190
AGCGGCAGGT CCCACCACGA GCCGTCATCA ACAGTGCAGG CTACAAAATC CTCACGTCCG TGGACCAATA 1260
CCTGGAGCTC ATTGGCAACT CCTTACCAGG GACCACGGCA AAGTCGGGCA GTGCCCCCAT CCTCAAGTGC 1330
CCCACACAGT TCCCGCTCAT CCTCTGGCAT CCTTATGCGC GTCACTACTA CTTCTGCATG ATGACAGAAG 1400
CCGAGCAGGA CAAGTGGCAG GCTGTGCTGC AGGACTGCAT CCGGCACTGC AACAATGGAA TCCCTGAGGA 1470
CTCCAAGGTA GAGGGCCCTG CGTTCACAGA TGCCATCCGC ATGTACCGAC AGTCCAAGGA GCTGTACGGC 1540
ACCTGGGAGA TGCTGTGTGG GAACGAGGTG CAGATCCTGA GCAACCTGGT GATGGAGGAG CTGGGCCCTG 1610
AGCTGAAGGC AGAGCTCGGC CCGCGGCTGA AGGGGAAACC GCAGGAGCGG CAGCGGCAGT GGATCCAGAT 1680
CTCGGACGCC GTGTACCACA TGGTGTACGA GCAGGCCAAG GCGCGCTTCG AGGAGGTGCT GTCCAAGGTG 1750
CAGCAGGTGC AGCCGGCCAT GCAGGCCGTC ATCCGAACTG ACATGGACCA AATTATCACC TCCAAGGAGC 1820
ACCTTGCCAG CAAGATCCGA GCCTTCATCC TCCCCAAGGC AGAGGTGTGC GTGCGGAACC ATGTCCAGCC 1890
CTACATCCCA TCCATCCTGG AGGCCCTGAT GGTCCCCACC AGCCAGGGCT TCACTGAGGT GCGAGATGTC 1960
TTCTTCAAGG AGGTCACGGA CATGAACCTG AACGTCATCA ACGAGGGCGG CATTGACAAG CTGGGCGAGT 2030
```

Figure 1B – Human STR_50E1 – SEQ ID NO:1

ACATGGAGAA GCTGTCCCGG CTGGCGTACC ACCCCCTGAA GATGCAGAGC TGCTATGAGA AGATGGAGTC 2100

GCTGCGACTG GACGGGCTGC AGCAGCGATT TGATGTGTCC AGCACGTCCG TGTTCAAGCA GCGAGCCCAG 2170

ATCCACATGC GGGAGCAAAT GGACAATGCC GTGTATACGT TCGAGACCCT CCTGCACCAG GAGCTGGGGA 2240

AGGGGCCCAC CAAGGAGGAG CTGTGCAAGT CCATCCAGCG GGTCCTGGAG CGGGTGCTGA AAAAATACGA 2310

CTACGACAGC AGCTCTGTGC GGAAGAGGTT CTTCCGGGAG GCGCTGCTGC AGATCAGCAT CCCGTTCCTG 2380

CTCAAGAAGC TGGCCCCTAC CTGCAAGTCG GAGCTGCCCC GGTTCCAGGA GCTGATCTTC GAGGACTTTG 2450

CCAGGTTCAT CCTGGTGGAA AACACGTACG AGGAGGTGGT GCTGCAGACC GTCATGAAGG ACATCCTGCA 2520

GGCTGTGAAG GAGGCCGCGG TGCAGAGGAA GCACAACCTC TACCGGGACA GCATGGTCAT GCACAACAGC 2590

GACCCCAACC TGCACCTGCT GGCCGAGGGC GCCCCCATCG ACTGGGGCGA GGAGTACAGC AACAGCGGCG 2660

GGGGCGGCAG CCCCAGCCCC AGCACCCCGG AGTCAGCCAC CCTCTCGGAA AAGCGACGGC GCGCCAAGCA 2730

GGTGGTCTCT GTGGTCCAGG ATGAGGAGGT GGGGCTGCCC TTTGAGGCTA GCCCTGAGTC ACCACCACCT 2800

GCGTCCCCGG ACGGTGTCAC TGAGATCCGA GGCCTGCTGG CCCAAGGTCT GCGGCCTGAG AGCCCCCCAC 2870

CAGCCGGCCC CCTGCTCAAC GGGGCCCCCG CTGGGGAGAG TCCCCAGCCT AAGGCCGCCC CCGAGGCCTC 2940

CTCGCCGCCT GCCTCACCCC TCCAGCATCT CCTGCCTGGA AAGGCTGTGG ACCTTGGGCC CCCCAAGCCC 3010

AGCGACCAGG AGACTGGAGA GCAGGTGTCC AGCCCCAGCA GCCACCCCGC CCTCCACACC ACCACCGAGG 3080

ACAGTGCAGG GGTGCAGACT GAGTTCTAGG CCAGTGGGTC CCTGACTGCT GCACATGGCA CAGGCCGTTC 3150

CCTTCCGGAC CCAGGCAGGC TCAGCTCTGG GGAGGGCACC CTGGTCTGTG CCTTGTGGGT GGAGGCGGGG 3220

CAGGGCTGTG TGGCACCGCC AGGGAGCGGG CCCACCTGAG TCACTTTATT GGGTTCAGTC AACACTTTCT 3290

TGCTCCCTGT TTTCTCTTCT GTGGGATGAT CTCAGATGCA GGGGCTGGTT TTGGGGTTTT CCTGCTTGTG 3360

CCAAGGGCTG GACACTGCTG GGGGGCTGGA AAGCCCCTCC CTTCCTGTCC TTCTGTGGCC TCCATCCCCT 3430

CATGGGTGCT GCCATCCTTC CTGGAGAGAG GGAGGTGAAA GCTGGTGTGA GCCCAGTGGG TTCCCGCCCA 3500

CTCACCCAGG AGCTGGCTGG GCCAGGACCG GGAGAGGGAG CACTGCTGCC CTCCTGGCCC TGCTCCTTCC 3570

GCAGTTAGGG GTGGACCGAG CCTCGCTTTC CCCACTGTTC TGGAGGGAAG GGGAAGGAGG GGGTCTTCAG 3640

GCTGGAGCCA GGCTGGGGGT GCTGGGTGGA GAGATGAGAT TTAGGGGGTG CCTCATGGGG TGGGCAGGCC 3710

TGGGGTGAAA TGAGAAAGGC CCAGAACGTG CAGGTCTGCG GAGGGGAAGT GTCCTGAGTG AAGGAGGGGA 3780

CCCCATCCTG GGGATGCTGG GAGTGAGTGA GTGAGATGGC TGAGTGAGGG TTATGGGGAG CCTGAGGTTT 3850

TATGGGCCTG TGTATCCCCT TCTCCCGGCC CCAGCCTGCC TCCCTCCTGC CCGCCTGGCC CACAGGTCTC 3920

CCTCTGGTCC CTGTCCCTCT GGTGGTTGGG GATGGAGCGG CAGCAAGGGG TGTAATGGGG CTGGGTTCTG 3990

TCTTCTACAG GCCACCCCGA GGTCCTCAGT GGTTGCCTGG GGAGCCGGAC GGGGCTCCTG AGGGGTACAG 4060

GTTGGGTGGG CCCTCCCTGA GGGTCTGGGG TCAGGCTTTG GCCTCTGCTG CCTCTCAGTC ACCAAGTCAC 4130

CTCCCTCTGA AAATCCAGTC CCTTCTTTGG ATGTCCTTGT GAGTCACTCT GGGCCTGGCT GTCGTCCCTC 4200

Figure 1C – Human STR_50E1 – SEQ ID NO:1

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CTCAGCTTCT TGTTCCTGGG ACAAGGGTCA AGCCAGGATG GGCCCAGGCN TGGGATCCCC CACCCCAGGA  4270
CCCCACAGGC CCCCTCCCCT GNTGNTTTGC GGGGGGCAGG GCAGAAATGG ACTCCTTTTG GGTCCCCGAG  4340
GTGGGGTCCC CTCCCAGCCC TGCATCCTCC GTGCCCTAGA CCTGCTCCCC AGAGGAGGGG CCTTGACCCA  4410
CAGGAAGTGT GGTGGCGCCT GGCAATCAGG GACCCCCAGC TGCCGCAGCC CTGGTTTTTG GCGCATCTTT  4480
TCCCTCTTGT CCCGAAGATT TGCGCCTTTA GTGCCTTTTG AGGGGTTCCC ATCATCCCTC CCTGATATTG  4550
TATTGAAAAT ATTATGCACA CTGTTCATGC TTTTACTAAT CAATAAACGC TTTATTTAAA AAAAAAAAAA  4620
AAA 4623
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EXHIBIT B

Figure 3A – Human STR_50E1 – SEQ ID NO:3

Nucleotide sequence of short splice variant

(Initiation ATG and stop codons are underlined)

GGGCTCCCTG CACAAATGCG TTGGGTGATG GGGGCTGAAT CCAGCCCACA CTGCACTTGC CAAGCCAGCT 70

GGGGCCCTGG CACAAGACAG TCCCAGCCTG TTTTCACTGA CTTTGCTAAT TCTCACGGAG GCACCATGTG 140

GTGTGGGAAG GCCCGGTCCT CGTAACCTCT CTGCTCCCAG GTCCCTGACC AGTCCTTAAC ACACAGTGGT 210

CTTTGCTCAC CTGCGGCCCA GCTCTGGGCT CTCCCCACAG CATCCTTTGC CTTGCCTCCC TCCCATCTTC 280

CTCTGGGCCT TCTCTCTGCT CCTGCCCAGG AAACTGTGCT CTCAGGAGCG CAGGAGCCAG CTCTCAGCCC 350

CCATCTCCTG GGCACTCACC GTACTCAGGA AATATGTTCT GAATTCAGGA TTATCCTCAT TCTACTGAGA 420

AGACCTGGAG GACAGAAATC AGCAAGACCT AAAGGGGAGA GGAAGGAGGG CCAGGCTGGG GTGGAGGTGC 490

CCCACCCGGG AGCCCGGGCG CAGCCTCACC GCAGGCTGAT TCACAGAAGG CTCAGAGGGT TGCGAGGGCC 560

CAATCGGCAC TGTCATCCTG CCCAGGCTCT GAGTCACCAG CTGGTGAGGG GCAGCTGCAG CCCAGCAGGA 630

AACAAAGTCT AGCATGGAAG AGGTGGGAGG GAGGTGGTGG GGCCTGAAAC CCCGCCTGGC TGGCCTTAGA 700

GGAACTGGGA GTGACTGTCC GGCACTGGCT CAGCAGCAAA CAGCTCTCAA GGACGTGCTA GGAGTCAGGA 770

ACTGGGCCAG CTCCGGTCCC TTCCTTTTGG GGCTCTCACT CTGGAGGATG GGGTGGATGG GAGAAAAAAC 840

CGGGAAGATC CTGACGGAGT TCCTCCAGTT CTATGAAGAC CAGTATGGCG TGGCTCTCTT CAACAGCATG 910

CGCCATGAGA TTGAGGGCAC GGGGCTGCCG CAGGCCCAGC TGCTCTGGCG CAAGGTGCCA CTGGACGAGC 980

GCATCGTCTT CTCGGGGAAC CTCTTCCAGC ACCAGGAGGA CAGCAAGAAG TGGAGAAACC GCTTCAGCCT 1050

CGTGCCCCAC AACTACGGGC TGGTGCTCTA CGAAAACAAA GCGGCCTATG AGCGGCAGGT CCCACCACGA 1120

GCCGTCATCA ACAGTGCAGG CTACAAAATC CTCACGTCCG TGGACCAATA CCTGGAGCTC ATTGGCAACT 1190

CCTTACCAGG GACCACGGCA AAGTCGGGCA GTGCCCCCAT CCTCAAGTGC CCCACACAGT TCCCGCTCAT 1260

CCTCTGGCAT CCTTATGCGC GTCACTACTA CTTCTGCATG ATGACAGAAG CCGAGCAGGA CAAGTGGCAG 1330

GCTGTGCTGC AGGACTGCAT CCGGCACTGC AACAATGGAA TCCCTGAGGA CTCCAAGGTA GAGGGCCCTG 1400

CGTTCACAGA TGCCATCCGC ATGTACCGAC AGTCCAAGGA GCTGTACGGC ACCTGGGAGA TGCTGTGTGG 1470

GAACGAGGTG CAGATCCTGA GCAACCTGGT GATGGAGGAG CTGGGCCCTG AGCTGAAGGC AGAGCTCGGC 1540

CCGCGGCTGA AGGGGAAACC GCAGGAGCGG CAGCGGCAGT GGATCCAGAT CTCGGACGCC GTGTACCACA 1610

TGGTGTACGA GCAGGCCAAG GCGCGCTTCG AGGAGGTGCT GTCCAAGGTG CAGCAGGTGC AGCCGGCCAT 1680

GCAGGCCGTC ATCCGAACTG ACATGGACCA AATTATCACC TCCAAGGAGC ACCTTGCCAG CAAGATCCGA 1750

GCCTTCATCC TCCCCAAGGC AGAGGTGTGC GTGCGGAACC ATGTCCAGCC CTACATCCCA TCCATCCTGG 1820

AGGCCCTGAT GGTCCCCACC AGCCAGGGCT TCACTGAGGT GCGAGATGTC TTCTTCAAGG AGGTCACGGA 1890

CATGAACCTG AACGTCATCA ACGAGGGCGG CATTGACAAG CTGGGCGAGT ACATGGAGAA GCTGTCCCGG 1960

CTGGCGTACC ACCCCCTGAA GATGCAGAGC TGCTATGAGA AGATGGAGTC GCTGCGACTG GACGGGCTGC 2030

Figure 3B – Human STR_50E1 – SEQ ID NO:3

AGCAGCGATT TGATGTGTCC AGCACGTCCG TGTTCAAGCA GCGAGCCCAG ATCCACATGC GGGAGCAAAT 2100

GGACAATGCC GTGTATACGT TCGAGACCCT CCTGCACCAG GAGCTGGGGA AGGGGCCCAC CAAGGAGGAG 2170

CTGTGCAAGT CCATCCAGCG GGTCCTGGAG CGGGTGCTGA AAAAATACGA CTACGACAGC AGCTCTGTGC 2240

GGAAGAGGTT CTTCCGGGAG GCGCTGCTGC AGATCAGCAT CCCGTTCCTG CTCAAGAAGC TGGCCCCTAC 2310

CTGCAAGTCG GAGCTGCCCC GGTTCCAGGA GCTGATCTTC GAGGACTTTG CCAGGTTCAT CCTGGTGGAA 2380

AACACGTACG AGGAGGTGGT GCTGCAGACC GTCATGAAGG ACATCCTGCA GGCTGTGAAG GAGGCCGCGG 2450

TGCAGAGGAA GCACAACCTC TACCGGGACA GCATGGTCAT GCACAACAGC GACCCCAACC TGCACCTGCT 2520

GGCCGAGGGC GCCCCCATCG ACTGGGGCGA GGAGTACAGC AACAGCGGCG GGGGCGGCAG CCCCAGCCCC 2590

AGCACCCCGG AGTCAGCCAC CCTCTCGGAA AAGCGACGGC GCGCCAAGCA GGTGGTCTCT GTGGTCCAGG 2660

ATGAGGAGGT GGGGCTGCCC TTTGAGGCTA GCCCTGAGTC ACCACCACCT GCGTCCCCGG ACGGTGTCAC 2730

TGAGATCCGA GGCCTGCTGG CCCAAGGTCT GCGGCCTGAG AGCCCCCCAC CAGCCGGCCC CCTGCTCAAC 2800

GGGGCCCCCG CTGGGGAGAG TCCCCAGCCT AAGGCCGCCC CCGAGGCCTC CTCGCCGCCT GCCTCACCCC 2870

TCCAGCATCT CCTGCCTGGA AAGGCTGTGG ACCTTGGGCC CCCCAAGCCC AGCGACCAGG AGACTGGAGA 2940

GCAGGTGTCC AGCCCCAGCA GCCACCCCGC CCTCCACACC ACCACCGAGG ACAGTGCAGG GGTGCAGACT 3010

GAGTTCTAGG CCAGTGGGTC CCTGACTGCT GCACATGGCA CAGGCCGTTC CCTTCCGGAC CCAGGCAGGC 3080

TCAGCTCTGG GGAGGGCACC CTGGTCTGTG CCTTGTGGGT GGAGGCGGGG CAGGGCTGTG TGGCACCGCC 3150

AGGGAGCGGG CCCACCTGAG TCACTTTATT GGGTTCAGTC AACACTTTCT TGCTCCCTGT TTTCTCTTCT 3220

GTGGGATGAT CTCAGATGCA GGGGCTGGTT TTGGGGTTTT CCTGCTTGTG CCAAGGGCTG GACACTGCTG 3290

GGGGGCTGGA AAGCCCCTCC CTTCCTGTCC TTCTGTGGCC TCCATCCCCT CATGGGTGCT GCCATCCTTC 3360

CTGGAGAGAG GGAGGTGAAA GCTGGTGTGA GCCCAGTGGG TTCCCGCCCA CTCACCCAGG AGCTGGCTGG 3430

GCCAGGACCG GGAGAGGGAG CACTGCTGCC CTCCTGGCCC TGCTCCTTCC GCAGTTAGGG GTGGACCGAG 3500

CCTCGCTTTC CCCACTGTTC TGGAGGGAAG GGGAAGGAGG GGGTCTTCAG GCTGGAGCCA GGCTGGGGGT 3570

GCTGGGTGGA GAGATGAGAT TTAGGGGGTG CCTCATGGGG TGGGCAGGCC TGGGGTGAAA TGAGAAAGGC 3640

CCAGAACGTG CAGGTCTGCG GAGGGGAAGT GTCCTGAGTG AAGGAGGGGA CCCCATCCTG GGGATGCTGG 3710

GAGTGAGTGA GTGAGATGGC TGAGTGAGGG TTATGGGGAG CCTGAGGTTT TATGGGCCTG TGTATCCCCT 3780

TCTCCCGGCC CCAGCCTGCC TCCCTCCTGC CCGCCTGGCC CACAGGTCTC CCTCTGGTCC CTGTCCCTCT 3850

GGTGGTTGGG GATGGAGCGG CAGCAAGGGG TGTAATGGGG CTGGGTTCTG TCTTCTACAG GCCACCCCGA 3920

GGTCCTCAGT GGTTGCCTGG GGAGCCGGAC GGGGCTCCTG AGGGGTACAG GTTGGGTGGG CCCTCCCTGA 3990

GGGTCTGGGG TCAGGCTTTG GCCTCTGCTG CCTCTCAGTC ACCAAGTCAC CTCCCTCTGA AAATCCAGTC 4060

CCTTCTTTGG ATGTCCTTGT GAGTCACTCT GGGCCTGGCT GTCGTCCCTC CTCAGCTTCT TGTTCCTGGG 4130

ACAAGGGTCA AGCCAGGATG GGCCCAGGCN TGGGATCCCC CACCCCAGGA CCCCACAGGC CCCCTCCCCT 4200

Figure 3C – Human STR_50E1 – SEQ ID NO:3

GNTGNTTTGC GGGGGGCAGG GCAGAAATGG ACTCCTTTTG GGTCCCCGAG GTGGGGTCCC CTCCCAGCCC 4270

TGCATCCTCC GTGCCCTAGA CCTGCTCCCC AGAGGAGGGG CCTTGACCCA CAGGAAGTGT GGTGGCGCCT 4340

GGCAATCAGG GACCCCCAGC TGCCGCAGCC CTGGTTTTTG GCGCATCTTT TCCCTCTTGT CCCGAAGATT 4410

TGCGCCTTTA GTGCCTTTTG AGGGGTTCCC ATCATCCCTC CCTGATATTG TATTGAAAAT ATTATGCACA 4480

CTGTTCATGC TTTTACTAAT CAATAAACGC TTTATTTAAA AAAAAAAAAA AAA 4533

EXHIBIT 1

School of Law

April 12, 2004

Re: U.S. Patent Application No. 10/612,318
Sylvia G. Kachalsky et al., "STR50 and uses thereof,"
Attorney Docket No. 2094/0878/67656-A/JPW/FHB

Sylvia G. Kachalsky, Inventor
c/o John P. White
Cooper & Dunham LLP
1185 Avenue of the Americas
New York NY 10036

Dear Ms. Kachalsky:

I am writing to call your attention to a printed publication that may constitute material prior art with respect to the above-referenced patent application.

Enclosed please find a copy of a CD-ROM document entitled "On the preparation and utilization of isolated and purified oligonucleotides," which I produced on March 9, 2002 and contributed to the public collection of the Kathrine R. Everett Law Library of the University of North Carolina on March 14, 2002.

For your convenience, I have also enclosed a hard copy of the initial portion of the text file stored on that CD-ROM. As you can ascertain from that excerpt, the CD-ROM reference contains a full written description of several million oligonucleotides of between 8 and 12 nucleotides in length inclusive, together with methods of making and using each.

I believe that the reference is material prior art at least with respect to one or more claims of the above-referenced application. Accordingly, I would recommend that the attorney or agent handling this application promptly disclose this reference to the Patent Office. As a courtesy, I would appreciate a written acknowledgement that he or she has done so.

If you wish to discuss this matter, I can be reached at the above phone number or by email at chin@unc.edu.

Sincerely yours,

Andrew Chin

Andrew Chin
Associate Professor

The University of North Carolina at Chapel Hill • CB# 3380 • Van Hecke-Wettach Hall

Applicants: Sylvia G. Kachalsky, et al.
U.S. Serial No.: 10/612,318
Filed: July 1, 2003

Exhibit 1

On the Preparation and Utilization of Isolated and Purified Oligonucleotides

Andrew Chin
University of North Carolina School of Law
March 9, 2002

The term "isolated" as used herein refers to a nucleotide sequence that has been manually produced and is separated from its native, in vivo, cellular environment and is present in the substantial absence of other biological molecules of the same type. The term "purified" as used herein for nucleotide sequences preferably means lacking significant quantities of other biological macromolecules of the same type (but water, buffers, and other small molecules, can be present).

Preparation of Isolated and Purified Oligonucleotides

As described in U.S. Patent No. 5,808,022 (issued Sept. 15, 1998) (William D. Huse), oligonucleotide synthesis proceeds via linear coupling of individual monomers in a stepwise reaction. The reactions are generally performed on a solid phase support by first coupling the 3' end of the first monomer to the support. The second monomer is added to the 5' end of the first monomer in a condensation reaction to yield a dinucleotide coupled to the solid support. At the end of each coupling reaction, the by-products and unreacted, free monomers are washed away so that the starting material for the next round of synthesis is the pure oligonucleotide attached to the support. In this reaction scheme, the stepwise addition of individual monomers to a single, growing end of an oligonucleotide ensures accurate synthesis of the desired sequence. Moreover, unwanted side reactions are eliminated, such as the condensation of two oligonucleotides, resulting in high product yields.

Oligonucleotides are constructed by conventional procedures such as those described in J. Sambrook et al., Molecular Cloning: A Laboratory Manual 10.42-.46 (3rd ed. 2001); K. Itakura et al., Synthesis and Use of Synthetic Oligonucleotides, 53 Ann. Rev. Biochemistry 323 (1984); M.D. Matteucci & M.H. Caruthers, Synthesis of Deoxynucleotides on a Polymer Support, 103 J. Am. Chem. Soc'y 3185 (1981); S.A. Narang, DNA Synthesis, 39 Tetrahedron 3 (1983). Oligonucleotide chains up to about 70 nucleotide residues long are preferably synthesized on automated synthesizers well known in the art (such as the Beckman Oligo 1000 or the Applied Biosystems ABI 392 DNA Synthesizer). Present-day DNA synthesizers are so efficient that oligonucleotides up to about 25 nucleotides in length generally do not contain significant quantities of truncated DNA fragments and hence do not require purification by gel electrophoresis. If necessary, however, purification of synthetic oligonucleotides can be achieved by one of several methods, as described in J. Sambrook, supra, at 10.48-49; including denaturing polyacrylamide gel electrophoresis, as described in J. Sambrook, supra, at 10.11-.16; T. Atkinson & M. Smith, Solid-Phase Synthesis of Oligodeoxyribonucleotides by the Phosphate-Triester Method, in Oligonucleotide Synthesis: A Practical Approach 35-82 (M.J. Gait ed. 1984).

Utilization of Oligonucleotides

As described in U.S. Patent No. 6,316,191 (issued Nov. 13, 2001) (Radoje T. Drmanac), hybridization depends on the pairing of complementary bases in nucleic acids and is a specific tool useful for the general recognition of informational polymers. Diverse research problems using hybridization of a synthetic oligonucleotide of known sequence include, amongst others, the different techniques of identification of specific clones from CDNA and genomic libraries, detecting single base pair polymorphisms in DNA, generation of mutations by oligonucleotide mutagenesis, and the amplification of nucleic acids in vitro from a single sperm, an extinct organism, or a single virus infecting a single cell.

Synthetic oligonucleotides of arbitrary nucleotide sequence are utilized in biological research, wherein oligonucleotides of specified length and random nucleotide sequence are synthesized using known procedures such as those described in Huse, supra; U.S. Patent No. 5,639,595 (issued June 17, 1997) (Christopher K. Mirabelli et al.). Arbitrary oligonucleotide primers of specified length may be used in the synthesis of cDNA probes from mRNA as described in Sambrook, supra, at 9.38-.40; J.G. Williams et al., DNA Polymorphisms Amplified By Arbitrary Primers Are Useful As Genetic Markers, 18 Nucleic Acids Research 6531 (1990), in the systematic evolution of ligands by exponential enrichment as described in U.S. Patent No. 6,331,398 (issued Dec. 18, 2001) (Larry Gold & Craig Tuerk); C. Tuerk & L. Gold, Systematic Evolution of High-Affinity RNA Ligands of Bacteriophage T4 DNA Polymerase in Vitro, 249 Science 505 (1990), and in sequencing by hybridization as described in Drmanac, supra. Preferably, oligonucleotide primers and probes are characterized by sequences of 8 to 20 nucleotides that have moderate G+C content, are free of homopolymeric runs and directly or inversely repeated regions.

The disclosures of all publications and patents set forth hereinbefore are expressly incorporated herein by reference.

Sequence Listing

The listing of sequences set forth hereinafter consists of all sequences of 8 to 12 nucleotides that have between 40 and 60 percent G+C content and are free of homopolymeric runs of 4 or more bases and directly or inversely repeated regions of 4 or more bases. Based on the the disclosures herein and the knowledge of a person of ordinary skill in the art, it will be apparent to such a person how to make and use an isolated and/or purified oligonucleotide characterized by any of the following nucleotide sequences: